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10/15/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: A.G. Uitterlinden et al. Attorney Docket No.: KILS117129

Application No.: 09/786,992 Group Art Unit: 1634

Filed: March 9, 2001 Examiner: S.A. Sakelaris

Title: METHOD FOR DETERMINING SUSCEPTIBILITY TO HEART DISEASE BY SCREENING POLYMORPHISMS IN THE VITAMIN D RECEPTOR GENE

RESPONSE TO RESTRICTION REQUIREMENT/
REQUEST FOR EXTENSION OF TIME

Seattle, Washington 98101

September 30, 2002

TO THE COMMISSIONER FOR PATENTS:

A. Restriction Requirement Transmittal

Transmitted herewith is a response to a restriction requirement in the above-identified application.

__X__ 1. No additional claim fee is required, as shown below.

_____ 2. The claim fee has been calculated as shown below.

COMPUTATION OF FEE FOR CLAIMS AS AMENDED

	Claims Remaining After Amendment		Highest Number Previously Paid For		Present Extra		Rate		Additional Fee
Total Claims	26	-	26	=	**0**	x	9	=	0
Independent Claims	4	-	4	=	**0**	x	42	=	0
	TOTAL								$0

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CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

B. Request for Extension of Time

Applicant respectfully requests that the shortened statutory period for response to the outstanding Restriction Requirement dated July 16, 2002, set to expire on August 16, 2002, be extended by 2 months, to expire on October 16, 2002. The enclosed check includes the 2-month extension fee of $200.00.

C. Fees Enclosed

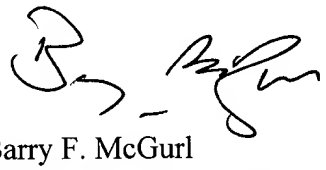
Enclosed is our Check No. 142388 in the amount of $200.00 to cover the amendment claim fee and request for extension of time fee.

D. Additional Fee Charges or Credit for Overpayment

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.18 which may be required during the entire pendency of the application, or credit any overpayment, to Deposit Account No. 03-1740. This authorization also hereby includes a request for any extensions of time of the appropriate length required upon the filing of any reply during the entire prosecution of this application. A copy of this document is enclosed.

Respectfully submitted,

CHRISTENSEN O'CONNOR
JOHNSON KINDNESS PLLC



Barry F. McGurl
Registration No. 43,340
Direct Dial No. 206.695.1775

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CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

BOX PATENT APPLICATION

#10
CD
10/15/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	A.G. Uitterlinden et al.	Attorney Docket No.:	KILS117129
Application No.:	09/786,992	Group Art Unit:	1634
Filed:	March 9, 2001	Examiner:	S.A. Sakelaris

Title: METHOD FOR DETERMINING SUSCEPTIBILITY TO HEART DISEASE BY SCREENING POLYMORPHISMS IN THE VITAMIN D RECEPTOR GENE

RESPONSE TO RESTRICTION REQUIREMENT

Seattle, Washington 98101

September 30, 2002

TO THE COMMISSIONER FOR PATENTS:

This communication is in response to the Office Action mailed July 16, 2002 (Paper No. 8), subjecting Claims 1-22 in the application to restriction. The Examiner has divided the Claims into three groups:

Group I (Claims 1-16), drawn to a method of determining susceptibility to heart disease in a subject;

Group II (Claims 17-19), drawn to methods of predicting the response of a subject to treatment; and

Group III (Claims 20-22), drawn to kits containing primers to amplify the vitamin D receptor gene.

Applicants elect Group II (i.e., Claims 17-19) with traverse, for initial prosecution in this application.

According to the Examiner, the inventions listed as Groups I, II and III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. More specifically, the Examiner has taken the view that while Group I and Group II share the common technical feature of amplification of

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1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

a portion of the vitamin D receptor gene, this special feature is not a contribution over the prior art in view of WO 97/40187 (Spector et al.). With respect to Group III, the Examiner has taken the view that the special technical feature, the vitamin D receptor gene, does not represent a contribution over the prior art in view of Spector. Therefore, the Examiner concludes there is no special technical feature linking Groups I, II and III which provides a contribution over the prior art as required by PCT Rule 13.2. Applicants respectfully request reconsideration and withdrawal of the restriction requirement for the following reasons.

An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single inventive concept. Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. 37 C.F.R. § 1.475(a) (underlining added).

Applicants submit that the claims of Groups I, II, and III share the common inventive concept that a subject's susceptibility to heart disease, and responsiveness to treatment therefor, can be predicted by analyzing the subject's genetic material and determining whether specific restriction enzyme site polymorphisms are present or absent in the vitamin D receptor gene.

Applicants submit that the special technical feature of the claims of Group I is "analyzing genetic material of a subject to determine which of the B/b, A/a or T/t alleles of the *BsmI*, *ApaI* or *TaqI* sites of the vitamin D receptor gene is/are present." The presence of the b, a or T allele(s) is/are associated with risk of heart disease.

Applicants submit that the special technical feature of the claims of Group II is identical to the special technical feature of the claims of Group I, *i.e.*, "analyzing genetic material of a

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CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

subject to determine which of the B/b, A/a or T/t alleles of the *BsmI*, *ApaI* or *TaqI* sites of the vitamin D receptor gene is/are present."

Applicants submit that the special technical feature of the claims of Group III is use of one or more nucleic acid primer molecules to amplify a portion of the vitamin D receptor gene, and thereby determine whether restriction enzyme site polymorphisms, that are known to be associated with susceptibility to heart disease, are present or absent. Applicant submits that this technical feature corresponds to the special technical feature of Claim Groups I and II.

Applicants submit that the foregoing common inventive concept, and special technical features, that link Groups I, II, and III, are a contribution over the teachings of Spector et al. (WO 97/40187) because Spector et al. do not teach or suggest the existence of restriction enzyme site polymorphisms that are predictive of susceptibility to heart disease. The teachings of Spector et al. are directed to restriction enzyme site polymorphisms in the vitamin D receptor gene that are predictive of susceptibility to osteoarthritis. Moreover, applicants note that Spector et al. teach the use of the *ApoI* restriction enzyme to detect polymorphisms in the vitamin D receptor gene that are predictive of the subject's susceptibility to osteoarthritis. In contrast, in some embodiments, the present invention utilizes the restriction enzyme *ApaI* to determine susceptibility to heart disease. The restriction enzymes *ApaI* and *ApoI* have different restriction sites, and are not interchangeable in the practice of the present invention.

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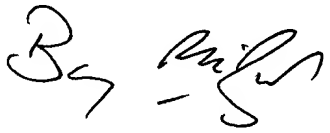
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

For the foregoing reasons, applicants respectfully submit that claims of Groups I, II, and III relate to a single general inventive concept, and possess the same or corresponding special technical features. Consequently, applicants respectfully request that the Examiner withdraw the restriction requirement.

Respectfully submitted,

CHRISTENSEN O'CONNOR
JOHNSON KINDNESS[PLLC]



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LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100